The Examiner recognizes that the specification provides working examples which demonstrate that the isolated antagonist peptides of SEQ ID NOs: 2, 5, 6, 17, and 24 inhibit IL-16 stimulated human T lymphocyte cell migration (see, for example pages 34-35). However, the Examiner contends that the specification does not provide any working examples that demonstrate that the isolated peptides of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32, and 34-38 are capable of inhibiting IL-16 mediated T lymphocyte migration. Therefore, the Examiner is of the opinion that in the absence of supporting evidence, the assumption that the peptides of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32 and 34-38 have biological activities similar to the antagonist peptides of SEQ ID NOs: 2, 5, 6, 17, and 24 cannot be accepted. In this regard, the Examiner has acknowledged Applicants' submission of additional data illustrating the efficacy of the IL-16 antagonistic peptide of SEQ ID NO: 26 (attached to the Amendment dated February 15, 2002 as Exhibit A). However, the Examiner states that such Exhibit is not proper evidence, since its content has not been peer-reviewed or attested to under 37 C.F.R. § 1.132.

In response to the Examiner's contentions, Applicants respectfully submit that the specification further teaches that the IL-16 antagonist peptides as instantly claimed share some common structural features. More specifically, these peptides substantially correspond to the C-terminal sequence of an IL-16 protein surrounding the Arg/Lys-Arg motif. See page 12, lines 19-25 of the specification, for example. Thus, the peptides as presently claimed all contain the Arg/Lys-Arg motif, and all correspond substantially to the C-terminal sequence of a naturally occurring IL-16 molecule.

The specification further teaches that these shared common structural characteristics are attributed to the function of these peptides of antagonizing an IL-16 molecule. For example, the specification teaches that in an IL-16 antagonist peptide, the replacement of the first Arg residue in the Arg/Arg motif with Ala, or the replacement of both Arg residues with Ala, completely abrogated the antagonist property of the peptide. See page 37 of the specification, for example. On the other hand, substitutions of residues adjacent to the Arg/Arg motif often do

not affect the antagonist activity of the peptide. See pages 34-35 of the specification, for example.

Based on these teachings of the present specification, those skilled in the art would appreciate that peptides of SEQ ID NOs: 3-4, 9-11, 13-16, 18-23, 25-32 and 34-38 have biological activities similar to the antagonist peptides of SEQ ID NOs: 2, 5, 6, 17, and 24.

As support of Applicants' position, Applicants provide herewith a Declaration of Dr. William Cruikshank under 37 C.F.R. § 1.132 (attached hereto as **Exhibit 1**). Dr. Cruikshank is one of the co-inventors named in the present application. In Paragraphs 5-6 of the Declaration, Dr. Cruikshank describes two experiments in which the functionality of peptides of SEQ ID NOS: 25-28, 32, 34-35 and 37 were tested. The results of these experiments indicate that these peptides effectively antagonized the biological effects of IL-16 in the IL-16 Induced Chemotaxis assay and the Mixed Lymphocyte Reaction assay. Together with SEQ ID NOs: 2, 5, 6, 17, and 24, Applicants have so far demonstrated the antagonistic activities of altogether thirteen (13) peptides, including three tetramers, one 6-mer, six 8-mers and three 16-mers.

In view of the foregoing, Applicants respectfully submit that based on the present teaching, those skilled in the art would be able to make the IL-16 antagonist peptides as instantly claimed, without undue experimentation. Applicants further maintain that the law does not require limitation of claims only to specifically exemplified subject matter, but permits a breadth of claimed subject matter which is consistent with the disclosure of the specification.

> First paragraph of 35 U.S.C. §112 does not require a specific example of everything within scope of broad Claim;...claims cannot be limited to specific examples, where there is clear disclosure of a broader invention.

In re Anderson,176 USPQ 331, 333 (CCPA 1973).

Accordingly, Applicants respectfully submit that the IL-16 antagonist peptides, as presently claimed, are supported by an enabled disclosure in full satisfaction of the requirements of 35 U.S.C. §112. As such, the rejection of claims 2-33 and 35 U.S.C. §112, first paragraph, is overcome. Withdrawal of the rejection is therefore respectfully requested.

With respect to the separate rejection of claim 35 under §112, first paragraph, the Examiner admits that the specification teaches a composition comprising an isolated IL-16 antagonist peptide consisting of the amino acid sequence of SEQ ID NOs: 2-7, 9-11, 13-32, and 34-38. However, the Examiner contends that the specification does not teach how to use an IL-16 "pharmaceutical" composition without undue experimentation for the treatment of a disease in an animal. The Examiner indicates that the rejection can be overcome by deleting the word "pharmaceutical" from the claims.

As to Applicants' previous submission that the present specification provides adequate teaching as to how to use the claimed pharmaceutical compositions at pages 26-28, the Examiner argues that this section of the specification merely provides a prophetic example, not a working example, of the formulation and administration of a "pharmaceutical" preparation of any IL-16 antagonist peptide.

The Examiner has also acknowledged Applicants' previous submission of a report, which illustrates the therapeutic effects of the peptides of SEQ ID NOs: 24 and 33 on antigen-induced early and late airway responses, airway hyperresponsiveness and airway inflammation in allergic sheep in Exhibit B, attached to the Amendment dated February 15, 2002. However, the Examiner states that such Exhibit is not proper evidence, since its content has not been peer-reviewed or attested to under 37 C.F.R. § 1.132.

In response, Applicants first respectfully submit that a principal feature of the present invention resides in the recognition of the antagonistic activities of peptides which substantially correspond to the C-terminal sequence of a full length IL-16 molecule. The specification teaches that an IL-16 antagonist peptide can be used in the treatment of an IL-16 mediated disorder, such as asthma, rheumatoid arthritis, inflammatory bowel disease, Graves' disease, multiple sclerosis, lupus and bullous pemphigoid. See pages 26-28 of the specification. Applicants admit that those skilled in the art may need to conduct additional experimentation to optimize the dosage and route of administration of a peptide in connection with the treatment of a particular disorder.

However, such additional experimentation is routine to those skilled in the art. Necessary experimentation is not determinative of the question of enablement; only undue experimentation is fatal under the provisions of 35 U.S.C. §112, first paragraph. In re Wands, 858 F.2d 731, 736-737, 8 U.S.P.Q. 1400, 1404 (Fed Cir. 1988).

As support of the enablement of the present specification and as evidence of the routine nature of additional experimentation, Applicants provide herewith a Declaration of Christopher P. Martin under 37 C.F.R. §1.132 (**Exhibit 2**). In his Declaration, Mr. Martin describes an experiment which was conducted to illustrate the therapeutic effects of the 8-mer peptide, RRKSLQSK (SEQ ID NO: 24), and the 16-mer peptide, RRKSLQSKETTAAGDS (SEQ ID NO: 33), on antigen-induced early and late airway responses, airway hyperresponsiveness and airway inflammation in allergic sheep.

As stated in Paragraph 7 of the Declaration, the results of the experiment demonstrate the therapeutic effects of IL-16 antagonist peptides in the treatment of asthma in an appropriate animal model. Significantly, Applicants observe that the methods used in these experiments, including measurement of airway mechanics, aerosol delivery, analysis of bronchoalveolar lavage fluid, and quantitating the antigen-induced responses, are all routine in nature and well known to those skilled in the art.

In view of the foregoing, Applicants respectfully submit that the pharmaceutical composition, as instantly claimed, is enabled by the present specification. Thus, it is respectfully submitted that the rejection of claim 35 under 35 U.S.C. §112, first paragraph, is overcome. Withdrawal of the rejection is therefore respectfully requested.

Claims 2-33 and 35 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Specifically, the Examiner alleges that the acronym and abbreviations "IL-16", "Arg", "Lys", "Thr", "Ala", "Ser", "Ile", "Val", "Leu" render the claims vague and indefinite.

Applicants respectfully submit that the term "IL-16" has been amended to recite "Interleukin-16 (IL-16)" in claim 2 where this term first appears in the claims.

Applicants further submit that the abbreviations "Arg", "Lys", "Thr", "Ala", "Ser", "Ile", "Val", "Leu", as recited in the claims, are abundantly clear to those skilled in the art as three letter codes for amino acids. It is also observed that numerous U.S. patents have issued which use three letter codes for amino acids in the claims.

In view of the foregoing, it is respectfully submitted that the rejection of the claims under 35 U.S.C. §112, second paragraph, is overcome. Withdrawal of the rejection is therefore respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the instant amendment. The attached page is captioned "**Version with Markings to Show Changes Made.**"

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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Enclosures: Version with Markings to Show Changes Made;
Exhibits 1-2.

Serial No: 09/368,630
Docket: 12875

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please amend claim 2 as follows:

2. (Twice Amended) An isolated Interleukin-16 (IL-16) antagonist peptide consisting of a sequence selected from the group consisting of RRKS (SEQ ID NO:2), RRTS (SEQ ID NO:3), KRKS (SEQ ID NO:4), RRAS (SEQ ID NO:5), RRKA (SEQ ID NO:6) and RRTA (SEQ ID NO:7).